Presentación de proyectos de investigación

Estudio 1

Estudio de la respuesta inmunitaria de pacientes con síndrome post-covid

Hai Z, Yang W, Martínez-Quiles N*

**Corresponding autor*

Introduction

Post-COVID syndrome (PCS) is characterized by persistent symptoms following SARS-CoV-2 infection, with immune dysregulation potentially contributing to its pathophysiology [1]. However, the underlying alterations in antibody responses and complement activity remain incompletely understood. We investigated SARS-CoV-2-specific humoral immunity, mucosal antibody responses, and complement components in patients with PCS compared with individuals who recovered from COVID-19 without persistent symptoms.

Methods

We studied a cohort of 104 PCS patients and COVID-recovered controls from the Community of Madrid, Spain. Serum antibodies against SARS-CoV-2 Nucleocapsid (N), full-length Spike, and receptor-binding domain (RBD) were assessed, including IgG subclasses. Salivary anti-N secretory IgA (sIgA) was quantified by ELISA. Complement components C3 and C4, factors B and H, total hemolytic activity (CH50), and circulating immune complexes were also measured. Analyses were performed considering vaccination history and SARS-CoV-2 reinfection status. Logistic regression and receiver operating characteristic (ROC) analyses were used to explore potential biomarkers of PCS.

Results

Compared with COVID-recovered controls, PCS patients exhibited significantly reduced serum anti-full-length Spike IgG, IgG1, IgG2, and IgG4 responses, while maintaining comparable anti-RBD IgG1 levels. Conversely, anti-N IgG responses were elevated in PCS patients, particularly following reinfection. Among PCS patients who received three vaccine doses and experienced reinfection, an enhanced anti-RBD IgG4/IgG1 switch was observed compared with their non-reinfected counterparts [2].

Further investigation revealed significantly increased salivary anti-N sIgA concentrations in PCS patients, indicating altered mucosal antibody responses. In parallel, serum C3 levels were significantly reduced, suggesting possible complement activation and consumption. C4 showed a nonsignificant decrease, whereas factors B and H, CH50 activity, and circulating immune complexes showed no significant differences between groups. ROC analysis demonstrated good discriminatory performance for C3 alone (AUC = 0.81); combining C3 with salivary anti-N sIgA further improved discrimination between PCS patients and COVID-recovered controls (AUC = 0.93; 95% CI: 0.88–0.98) [3].

In exploratory analyses of seropositive samples, anti-EBV IgG levels were significantly elevated in PCS patients compared with pre-pandemic controls, with a lower proportion of low-rank responses (31.7% vs. 67.9%, P = 0.0005) and a higher proportion of medium-rank responses (46.5% vs. 17.9%, P = 0.0062).

Discussion and conclusions

Our findings demonstrate that PCS is associated with distinct alterations in systemic and mucosal antibody responses, together with dysregulation of the complement system. Reduced anti-Spike antibody responses, preserved anti-RBD IgG1, increased anti-N antibodies, and reduced serum C3 levels suggest that multiple components of humoral immunity are affected in PCS. The combined assessment of salivary anti-N sIgA and serum C3 may provide a promising approach for identifying candidate biomarkers, although independent validation is required. These results contribute to understanding the immunological mechanisms underlying PCS and highlight the importance of further investigating complement dysregulation and persistent antiviral immune responses.

References

1. Altmann DM, Whettlock EM, Liu S, Arachchillage DJ, Boyton RJ. The immunology of long COVID. Nat Rev Immunol. 2023;23(10):618-34. doi: 10.1038/s41577-023-00904-7

2. Rossi N, Benítez-Cruz J, Marín-García P, Azcárate IG, González-Escalada A, Hervás OG, et al. Post-COVID syndrome patients show reduced anti-Spike antibodies compared to COVID-recovered controls, but enhanced IgG4/IgG1 switch after the third vaccine dose. Front Immunol. 2025;16:1670324. doi: 10.3389/fimmu.2025.1670324

3. Hai Z, Yang W, Ghazi A, Buitrago A, Marín-García P, Azcárate IG, et al. Increased anti-nucleocapsid secretory IgA and consumption of complement component 3 in post-COVID syndrome patients. Front Immunol. 2026;17:1822171. doi: 10.3389/fimmu.2026.1822171

Presenta: Narcisa Martínez-Quiles. Universidad Complutense de Madrid